REMARKS

Upon entry of the present Amendment, claims 85-86, 89, 94, 97-98, 100, 102, and 104-114 are pending and under examination. In the present Amendment, Applicants have canceled claims 87-88, 90-93, 95-96, 99, 101 and 103 without prejudice or disclaimer as being drawn to non-elected inventions. Applicants have amended the dependencies of claims 89, 98, 105, 106, and 108. Applicants have amended claims 94 and 97 to recite "that specifically binds to human STOP-1." That amendment is supported by the specification, e.g., at page 43, lines 18-21, and Figure 2. Applicants have added new claims 112-114, which read on the elected invention. Support for new claim 112 is found in the specification, e.g., at page 28, line 34, through page 29, line 8; and page 154, lines 2-5. Support for new claim 113 is found in present claim 94. Support for new claim 114 is found in the specification, e.g., in the paragraph bridging pages 41-42. No new matter is added by any of the foregoing amendments.

Applicants bring to the Examiner's attention co-pending, co-owned U.S. Application No. 11/929,465, filed 10/30/2007, published as US 2009/0136997 A1, and to the contents of the filewrapper of that application, including the pending claims and any Office Actions issued in that application.

I. Rejection of Claims 94, 97, and 98 Under 35 U.S.C. 112, 1st Paragraph

The Examiner rejected claims 94, 97, and 98 under the enablement requirement of 35 USC 112, first paragraph. (Office Action at page 3, item 6.) According to the Examiner:

> [t]he specification, while being enabling for a STOP-1 monoclonal antibody comprising all 6 CDRs (3 from the light and 3 from the heavy chain), does not reasonably provide enablement for a monoclonal antibody comprising just one CDR from the variable heavy chain (Claim 94), one variable heavy chain, or just one variable light chain…The claims are drawn to an antibody comprising less than all 6 CDRs. As claimed these molecules would not bind to the antigen.

(*Id.*) Applicants respectfully disagree. The Examiner's position is not in accord with prior representations by the Office, nor is it consistent with the enablement provided by the specification.

Claims 94 and 97 a drawn to "[a] monoclonal antibody that specifically binds to human STOP-1…" Claim 94 part (i), recites "a monoclonal antibody comprising (a) a V_H-CDR1 comprising the amino acid sequence of TINNYD (SEQ ID NO:14); (b) a V_H-CDR2 comprising the amino acid sequence of GYISPPSGATY (SEQ ID NO:15); and (c) a V_H-CDR3 comprising the amino acid sequence CARMVGMRRGVMDY (SEQ ID NO:16)…." (Contrary to the Examiner's contention above, claim 94 requires three V_H CDRs and not "just one CDR" from the variable heavy chain.) Claim 97 recites "[a] monoclonal antibody…that comprises the amino acid sequence of the heavy chain of FIG.31 (amino acids 21-251 of SEQ ID NO:105)." Claim 98 depends from claim 97 and further recites "(a) the light chain of FIG.27 (amino acids 24-239 of SEQ ID NO:92); or (b) the light chain of FIG.33 (amino acids 20-233 of SEQ ID NO:110).

Consistent with previous representations by the Office, recitation of the three V_H-CDR sequences in claim 94, part (i), or recitation of the heavy chain region of claim 97 is sufficient to enable one skilled in the art to make and use the claimed invention without undue experimentation. Applicants refer the Examiner to the attached presentation given by Larry Helms, USPTO SPE, Art Unit 1643, at the

Biotechnology/Chemical/Pharmaceutical Customer Partnership on June 13, 2007, entitled "Enablement Issues in the Examination of Antibodies" (referred to hereinafter as the "Presentation").[1] As indicated in slides 12-15, a claim to an antibody that (1) binds a specific antigen and (2) comprises a defined variable heavy chain domain sequence is enabled. According to the Presentation: "[i]n light of the prior art disclosing methods of obtaining antibodies that bind an antigen by screening complementary variable domain libraries, the specification's disclosure of an antibody that binds a specific antigen comprising a defined VH ...sequence would provide enough structure for one skilled in the art to practice the invention." (Slide 15, emphasis in original.) The Presentation relies on scientific publications demonstrating that antibodies that bind a specific antigen can be produced by using a specific V_H domain alone to screen a library of complementary (V_L) variable domains. (See Presentation, Slide 14.) Claims 94 and 97 are analogous to the example provided in the Presentation and are thus enabled.

The working examples described in the specification are consistent with and demonstrate the principles set forth in the Presentation. Example 16 (starting at page 154 of the specification) describes how phage-derived antibodies that bind STOP-1 were generated. The starting phagemid vectors (termed pV0350-2b and pV0350-4) contained sequence encoding humanized 4D5-8 antibody, which binds to an antigen called Her-2. (See specification at page 155, lines 4-30.) To generate a library for screening for anti-STOP-1 antibodies, the phagemid vectors were mutated only in the

[1] The agenda for that meeting is found at: http://www.uspto.gov/patents/init_events/bcp/bcpcp61307.jsp. Applicants obtained a copy of the Presentation by following a link provided by the USPTO to an outside web server:
http://www.uspto.gov/cgi-bin/exitconf/internet_exitconf.pl?target=www.cabic.com/bcp/.

sequences encoding the heavy chain variable regions. (See specification, paragraph bridging pages 155-156.) Therefore, the specificity for STOP-1 of the phage-derived antibodies that were isolated using that mutagenesis and screening strategy is determined by the heavy chain variable sequences. (Note that the light chain of antibody F5 (shown in Fig. 31) from amino acids 24-238 of SEQ ID NO:104 and the light chain of antibody S4 (shown in Fig. 33) from amino acids 19-233 of SEQ ID NO:110 share the same amino acid sequence, including all three V_L-CDRs, even though antibodies F5 and S4 bind to different epitopes of STOP-1 and have different activities.)

Accordingly, the present specification would reasonably enable one skilled in the art to make and use the antibody of claim 94 (for example, one skilled in the art could construct a V_H domain using the recited V_H CDR sequences along with framework regions well known to those skilled in the art) and the antibody of claim 97. Thus, the specification enables claims 94 and 97, as well as dependent claim 98, which depends from claim 97. Withdrawal of the rejection of claims 94 and 97-98 under the enablement requirement of 35 USC 112, first paragraph, is respectfully requested.

II. Rejection of Claims 85, 86, 89, and 105-111 Under 35 USC 102(a)

The Examiner rejected claims 85, 86, 89, and 105-111 as allegedly being anticipated by Monahan et al. (WO 2002/071928) ("Monahan"). (Office Action at page 6, item 10.) According to the Examiner, "Monahan et al. teach the STOP-1 protein (M450).... Monahan et al. discloses monoclonal antibodies specific for the said STOP-1 protein...." (*Id.* at item 12.) Applicants respectfully traverse this rejection.

Claim 85 recites "[a] monoclonal antibody that specifically binds to amino acids 33-52 or 33-53 of human STOP-1." To anticipate a claim, a reference must disclose each and every element of the claim. (See, e.g., MPEP 2131.) Monahan generally discloses a large genus of antibodies that bind to M450 (among other "marker proteins"), e.g., at page 10, last paragraph, and page 57, first paragraph, without identifying any specific region of STOP-1 to which such antibodies bind, let alone the specific region of STOP-1 as recited in claim 85 (i.e., from amino acids 33-52 or 33-53). Therefore, claim 85 represents a novel species of anti-STOP-1 antibodies that is not anticipated by the genus of anti-STOP-1 antibodies generally discussed by Monahan.

Moreover, the genus taught by Monahan does not render obvious the species of claim 85. One factor to consider in making this assessment is whether it would have been obvious "to select the claimed species or subgenus from the disclosed prior art genus." (MPEP 2144.08(II)(A)(4).) The size of the prior art genus is also to be considered. (*Id.*) Here, the size of Monahan's genus of anti-STOP-1 antibodies is large, and Monahan provides no motivation to select anti-STOP-1 antibodies that bind to the specific region of STOP-1 recited in claim 85. Any such motivation comes from Applicants' disclosure, which describes isolation of two antibodies, "6B12" and "F5," that bind to that specific region and that have a particular biological effect (i.e., a blocking effect). (See specification at page 154, lines 14-15; page 162, lines 8-9; and page 172, lines 9-10.) That biological effect is distinct from that of other anti-STOP-1 antibodies, which bind to a different STOP-1 region and which have a potentiating effect. (See specification, e.g., at page 166, lines 13-14, and page 170, lines 17-19.)

Thus, for at least the above reasons, Monahan cannot anticipate claim 85, and therefore cannot anticipate dependent claims 86, 89, and 105-111. Withdrawal of the rejection of claims 85, 86, 89, and 105-111 under 35 USC 102(a) is respectfully requested.

III. Allowable Subject Matter

Applicants acknowledge that the Examiner has found that claims 100, 102, and 104 are free of the prior art and allowable. (Office Action at page 6, item 14.)

CONCLUSION

For the reasons set forth above, Applicants believe that all pending claims are in condition for allowance. Should the Examiner believe that a telephone interview would expedite the prosecution of this application, Applicants invite the Examiner to call the undersigned at the telephone number indicated below.

Respectfully submitted,

GENENTECH, INC.

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By: /Danielle M. Pasqualone/
Danielle M. Pasqualone, Reg. No. 43,847
Phone: (650) 467-0594
Fax: (650) 952-9881